# Hypersensitivity Reactions

Immunology Unit
Department of Pathology
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**Lecture # 5/6**
**Foundation Block**

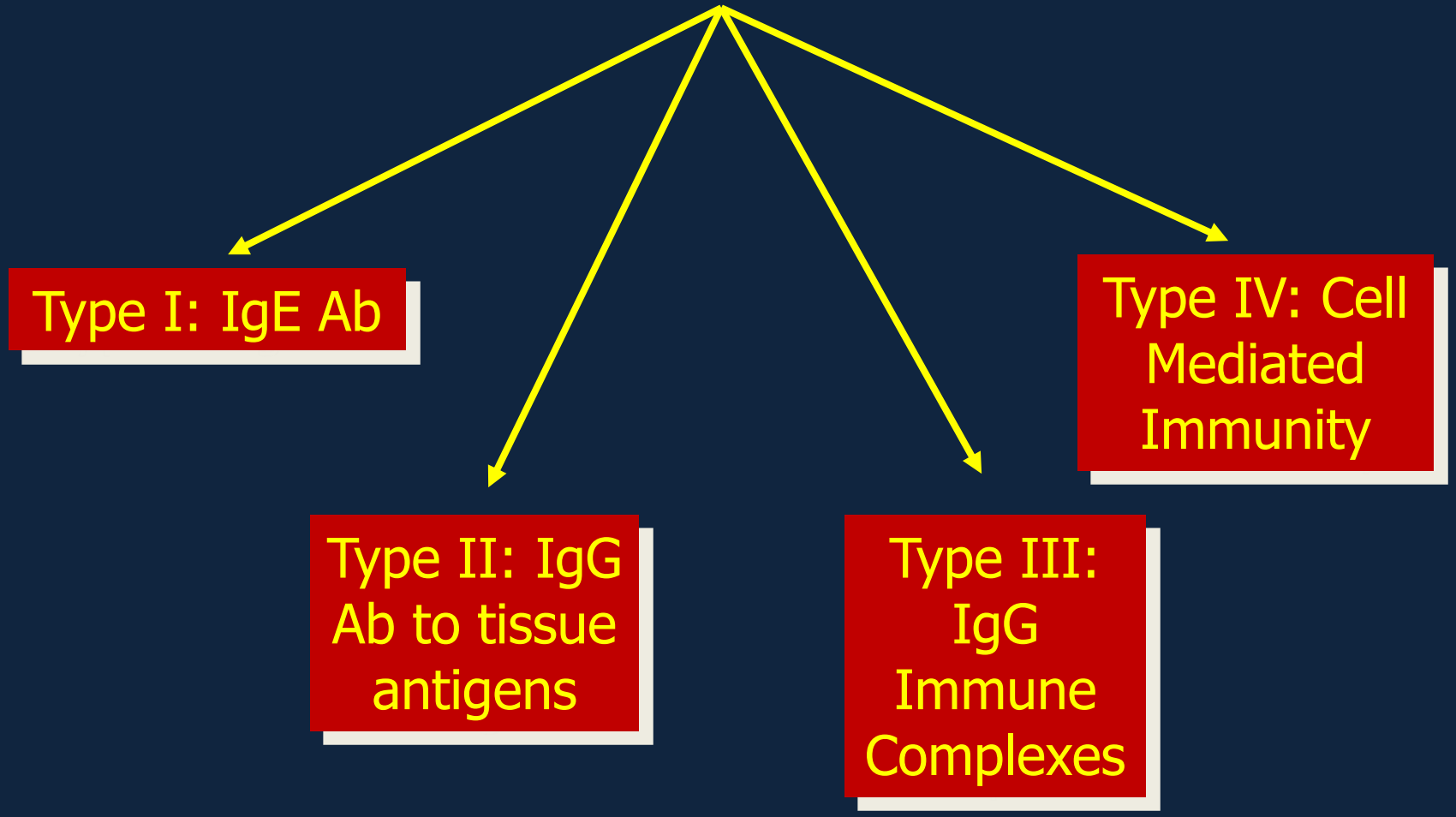
# Objectives

- To know that hypersensitivity reactions are over and excessive immune responses that can be harmful to body in four different ways
- To be familiar with inflammatory processes in Type I hypersensitivity reaction that mediates allergic inflammation
- Recognize that Type II hypersensitivity deals with immune responses against antigens that are integral part of cell membrane and are usually associated with autoimmune disorders
- To know that Type III hypersensitivity reactions are mediated by immune complexes and cause vasculitis
- Describe Type IV hypersensitivity is a purely cell mediated immune response associated with chronic inflammation

# What is hypersensitivity?

- **Protective immunity**: desirable reaction
- **Hypersensitivity**: undesirable reaction
- Undesirable responses can be mediated by
  - ***Antibody binding*** to antigens (Types I-III)
  - ***Cell mediated reaction*** to chemicals or proteins (Type IV)

# Gel and Coombs Classification



# Type I: Immediate Hypersensitivity

- Most people will not react to these allergens but some individuals "***atopic***" respond by producing large amounts of IgE

- Non-allergic individuals respond to these allergens by producing IgG antibodies

# Type I Hypersensitivity

- Also termed as:

  Immediate Hypersensitivity

  Anaphylactic reactions

  Allergic reactions

  (Occurs within minutes to hours)

# Features

- Antibody type: IgE

- Cellular components:

  Mast cells, basophiles & eosinophils

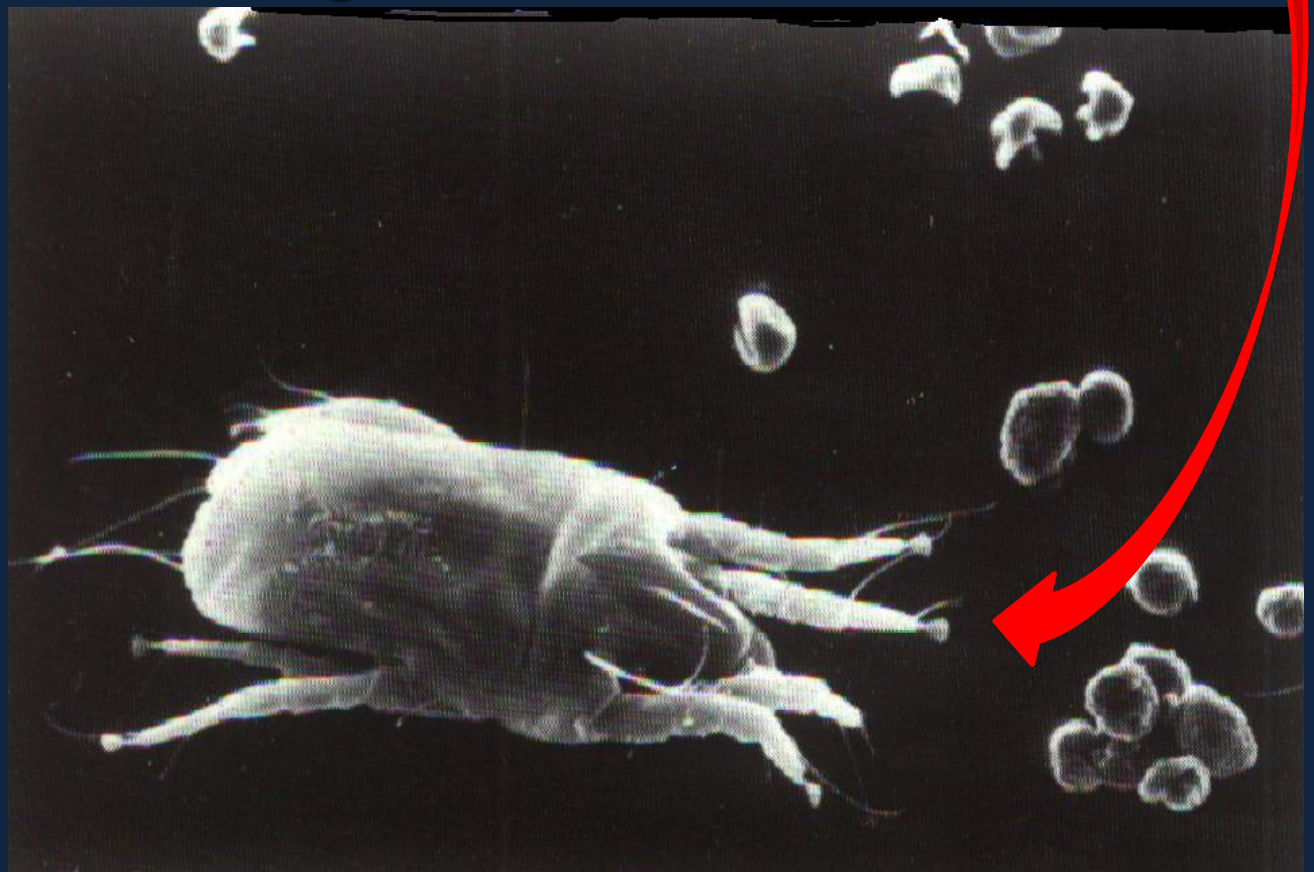
- Antigens:

  Also known as allergens

  (antigens with low molecular weight & highly soluble)

# Allergens

- Some of the allergens involved in type I hypersensitivity are: pollens, dust mite allergens, animal dander, nuts, shellfish, various drugs etc



# Type I reactions occur in two phases

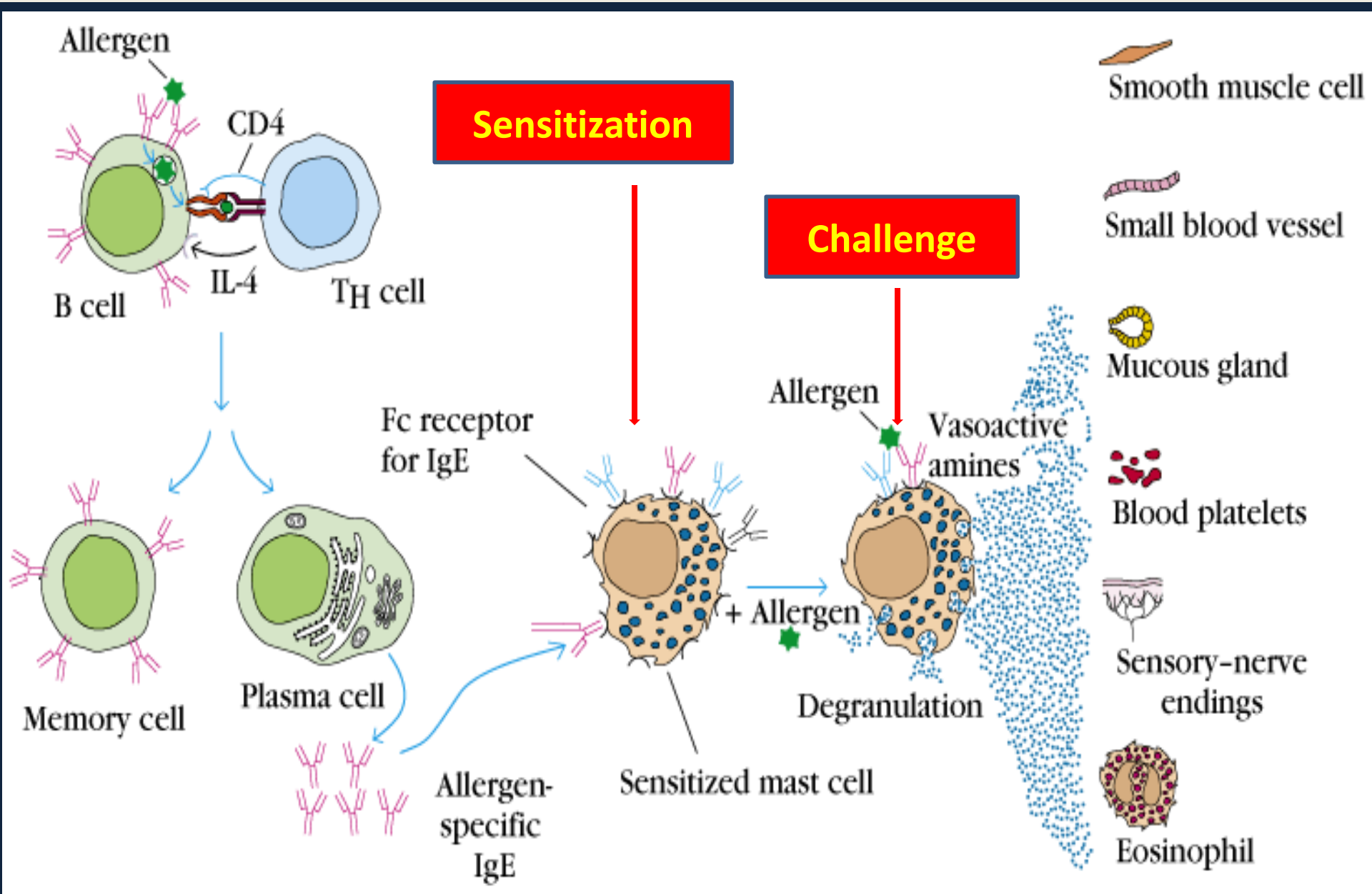
- **Sensitization phase**

  First contact with allergens

- **Challenge phase**

  Subsequent contact with allergens

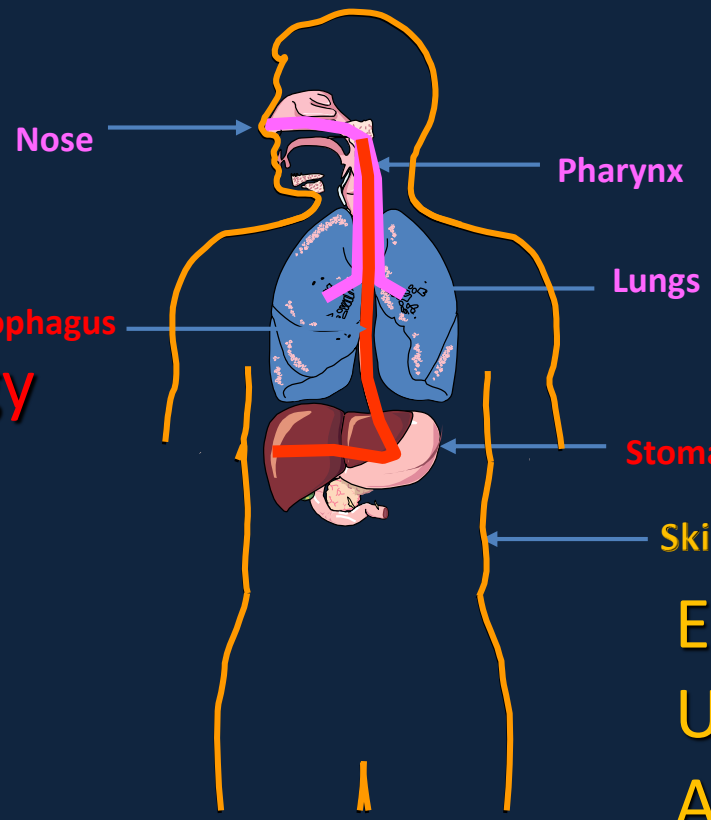
# Type I Hypersensitivity (Immediate)



# Primary and Secondary Mediators

| Mediator | Effects |
|---|---|
| | PRIMARY |
| Histamine, heparin | Increased vascular permeability; smooth-muscle contraction |
| Serotonin | Increased vascular permeability; smooth-muscle contraction |
| Eosinophil chemotactic factor (ECF-A) | Eosinophil chemotaxis |
| Neutrophil chemotactic factor (NCF-A) | Neutrophil chemotaxis |
| Proteases | Bronchial mucus secretion; degradation of blood-vessel basement membrane; generation of complement split products |
| | SECONDARY |
| Platelet-activating factor | Platelet aggregation and degranulation; contraction of pulmonary smooth muscles |
| Leukotrienes (slow reactive substance of anaphylaxis, SRS-A) | Increased vascular permeability; contraction of pulmonary smooth muscles |
| Prostaglandins | Vasodilation; contraction of pulmonary smooth muscles; platelet aggregation |
| Bradykinin | Increased vascular permeability; smooth-muscle contraction |
| Cytokines | |
| IL-1 and TNF-α | Systemic anaphylaxis; increased expression of CAMs on venular endothelial cells |
| IL-2, IL-3, IL-4, IL-5, IL-6, TGF-β, and GM-CSF | Various effects (see Table 12-1) |

# Allergy is a systemic disorder

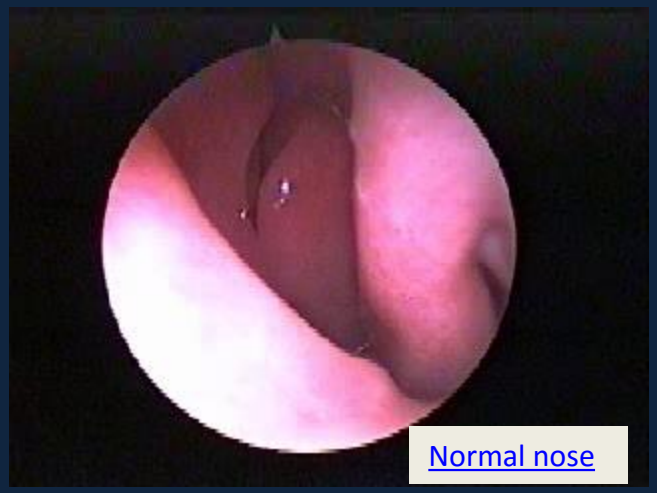



Allergic rhinitis
Asthma

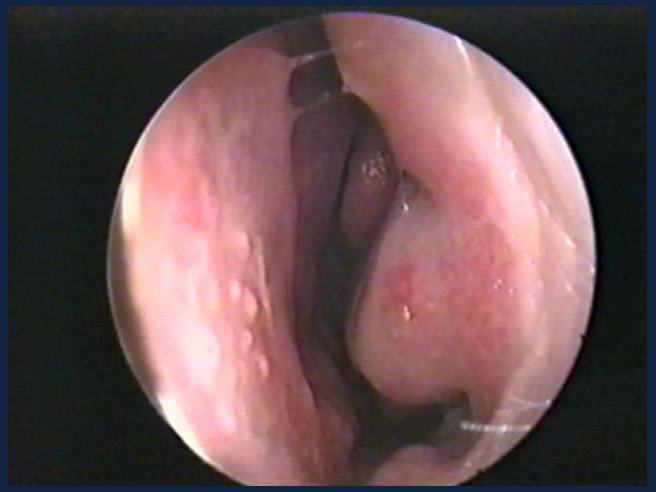
Food allergy

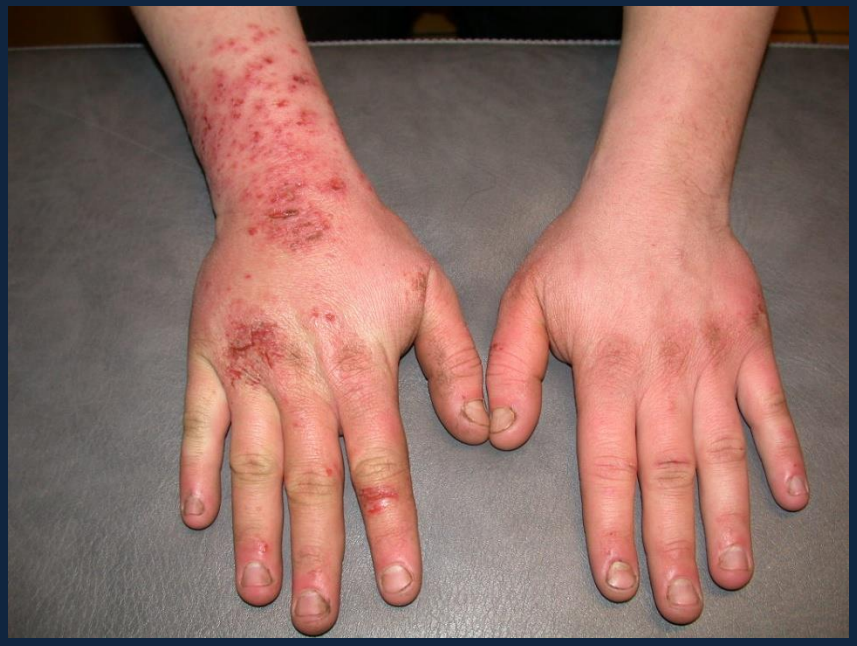
Eczema
Urticaria
Allergic dermatitis

# Allergy: Rhinitis, Eczema & Conjunctivitis



Normal nose





* Injected allergens:

Bee sting venom enters the blood stream

→ Systemic inflammation

→ Anaphylactic shock (life - threatening)

❖ Anaphylactoid reactions:-

Are non - IgE mediated

may result from contrast media or local anesthetics

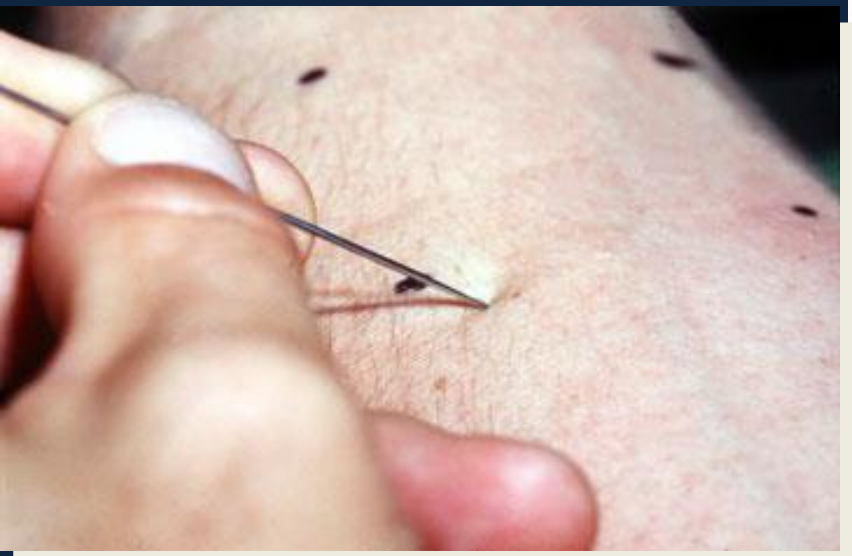
# Diagnosis of Allergy

## Skin Prick test

1. Skin prick test (SPT)

2. Specific IgE measurement (RAST)

3. Elimination / Provocation test (Food allergy)



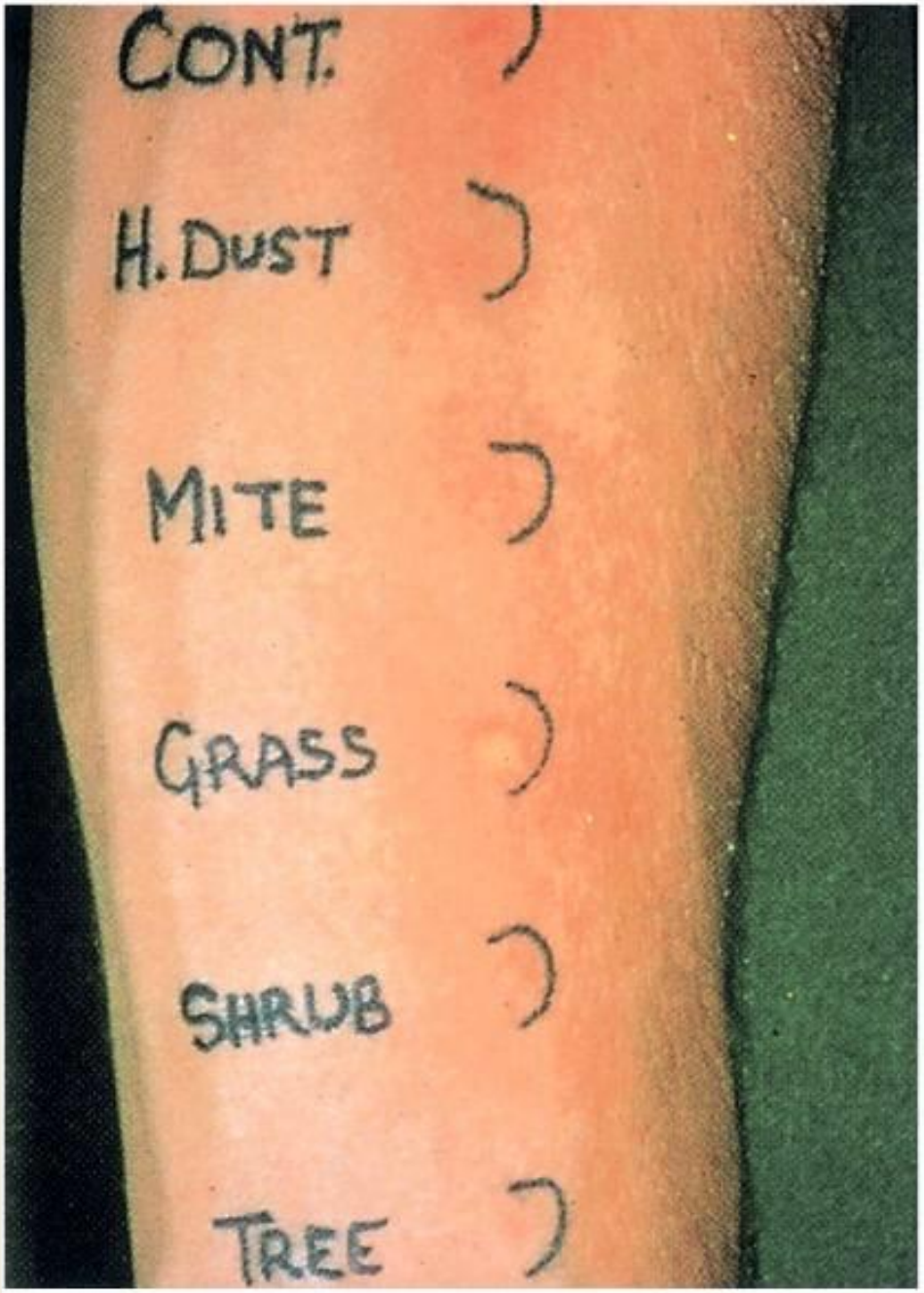
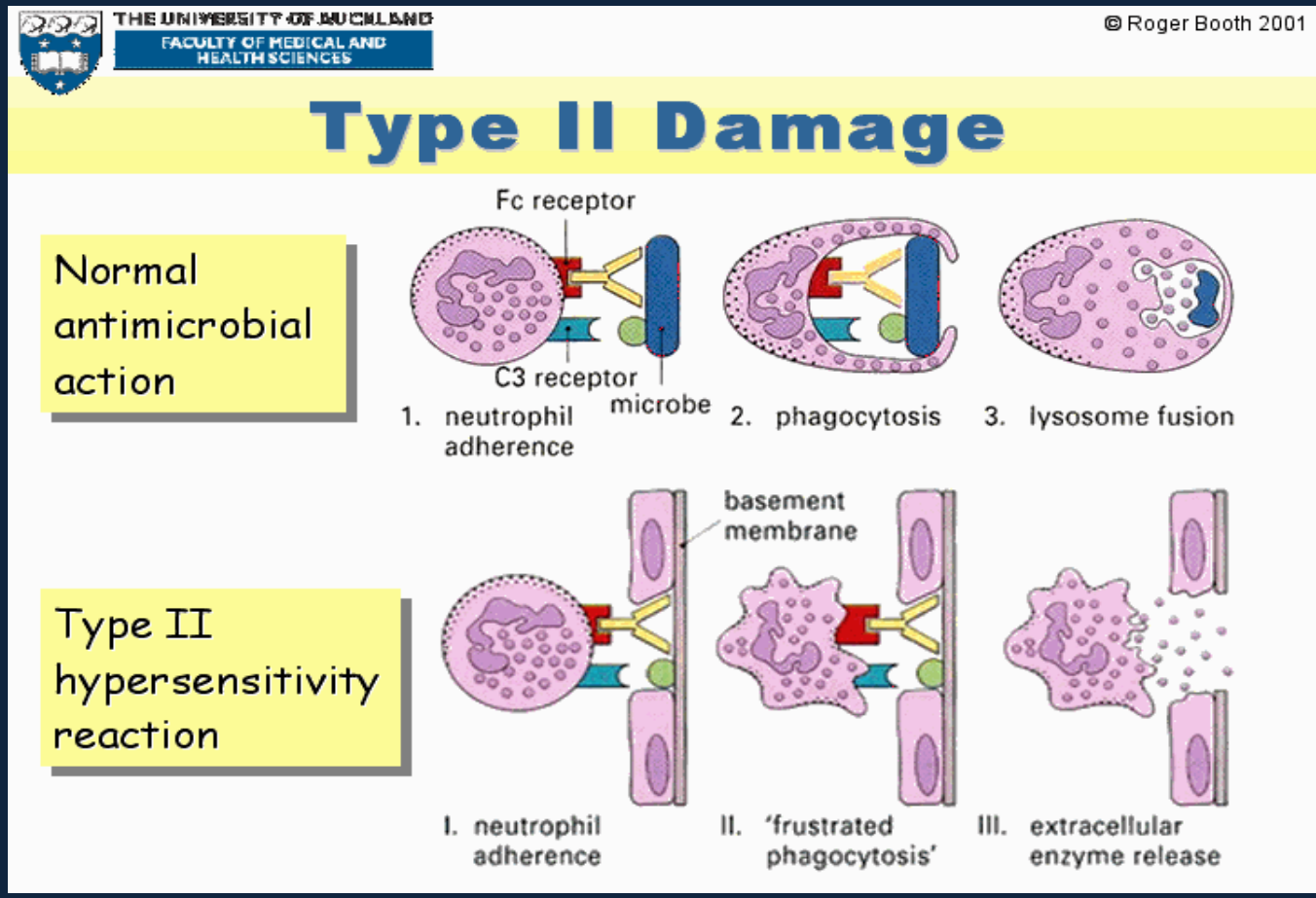



**Figure 15-10**
***Kuby IMMUNOLOGY, Sixth Edition***

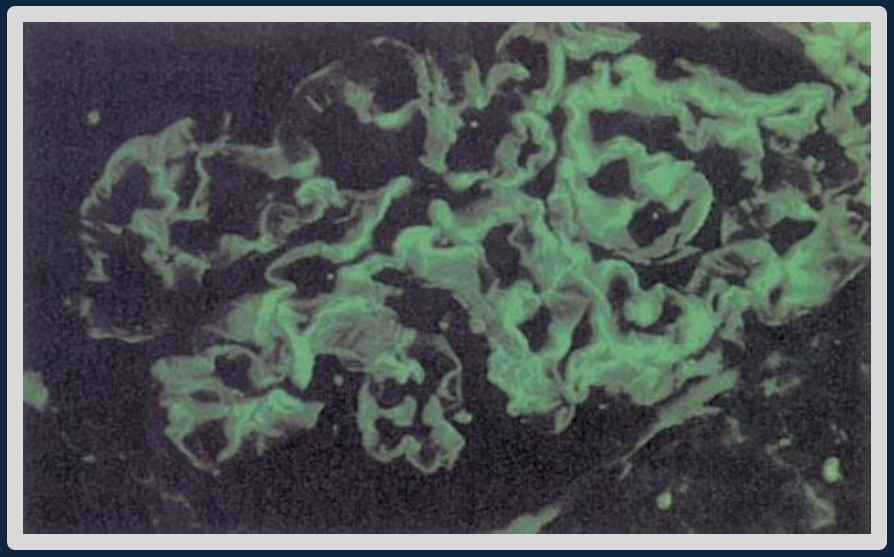
# Type II Hypersensitivity Reactions

- Features:-
  - IgG (or IgM)
    - Antigens: bound to cell membranes
      (Self antigens)
    - Exogenous antigens
      (microbial)
    - Complement activation
      (Invariable)



# Clinical examples:

Glomerulonephritis (anti-glomerular basement membrane)



Mis-matched blood transfusion

## Diagnosis

- Detection of antibodies and antigens by Immunofluoresence in tissue biopsy specimens e.g. kidney, skin etc.

# Type III: Immune complex hypersensitivity

- When an antigen reacts with an antibody the product they form is called an immune complex which is capable of inducing an inflammatory response

- Immune complexes are deposited in tissues like kidneys (nephritis), joints (arthritis) or blood vessels (vasculitis)

# Type III Hypersensitivity (immune–complex mediated)

- Features

**Antibody (IgG/ or IgM) + Antigen (soluble)**

↓

- Immune – Complex formation

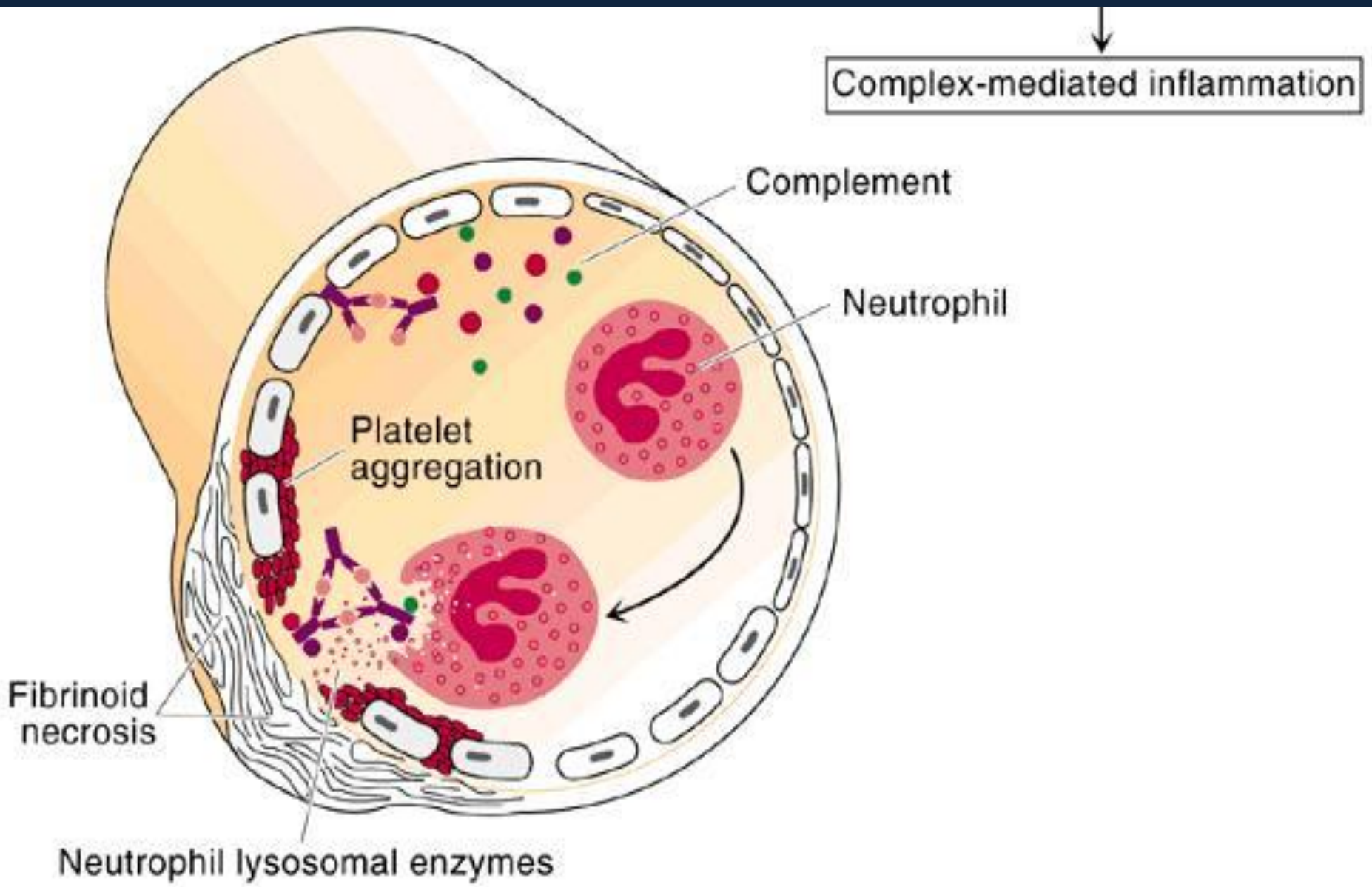
↓

- Complement activation

↓

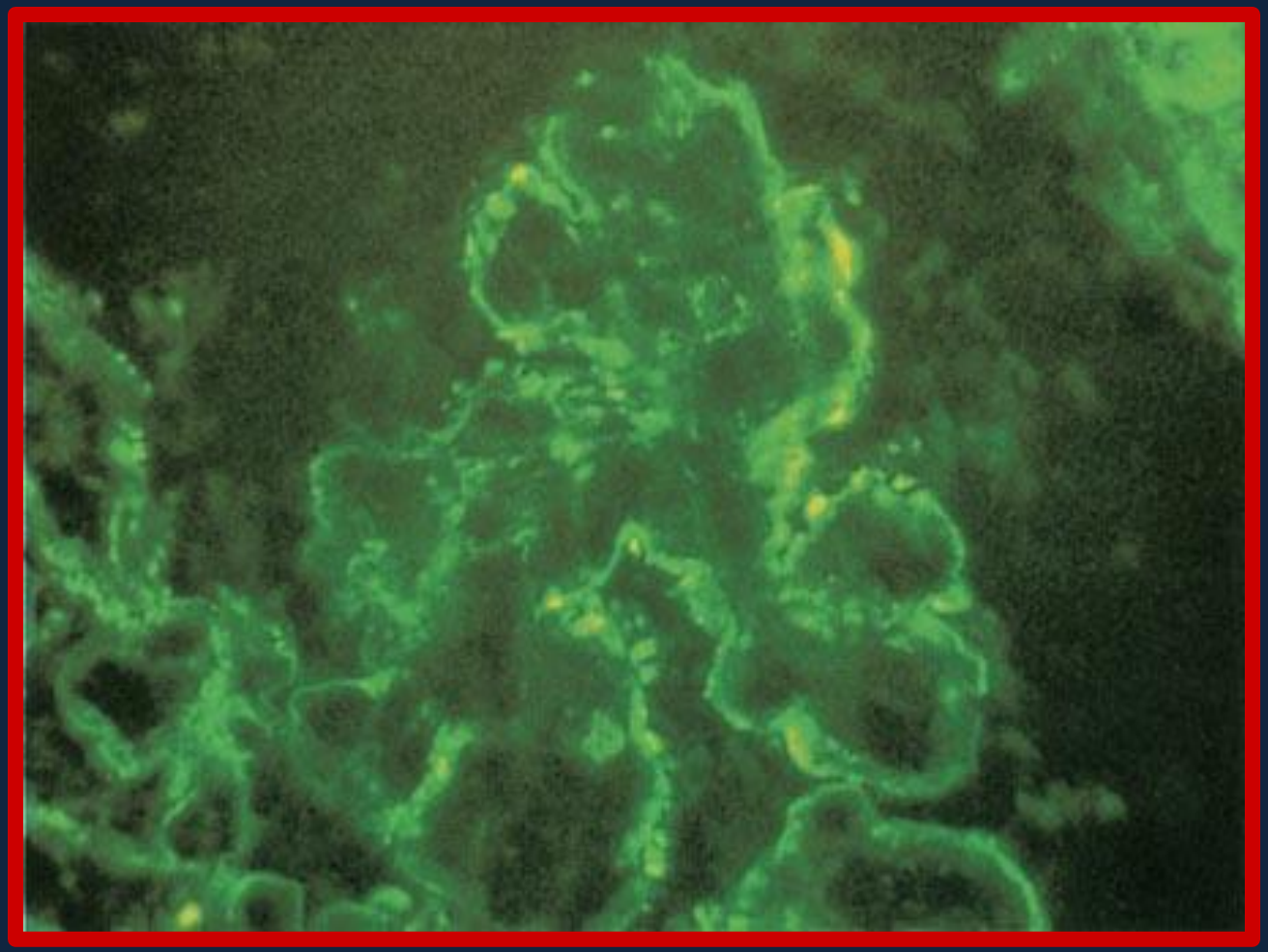
- Attraction of inflammatory cells

# Type III Reactions



# Type III Hypers. Reactions
# Clinical examples:

Glomerulonephritis: Rheumatoid arthritis, SLE



# Diagnosis of Type III Hypers. Reactions

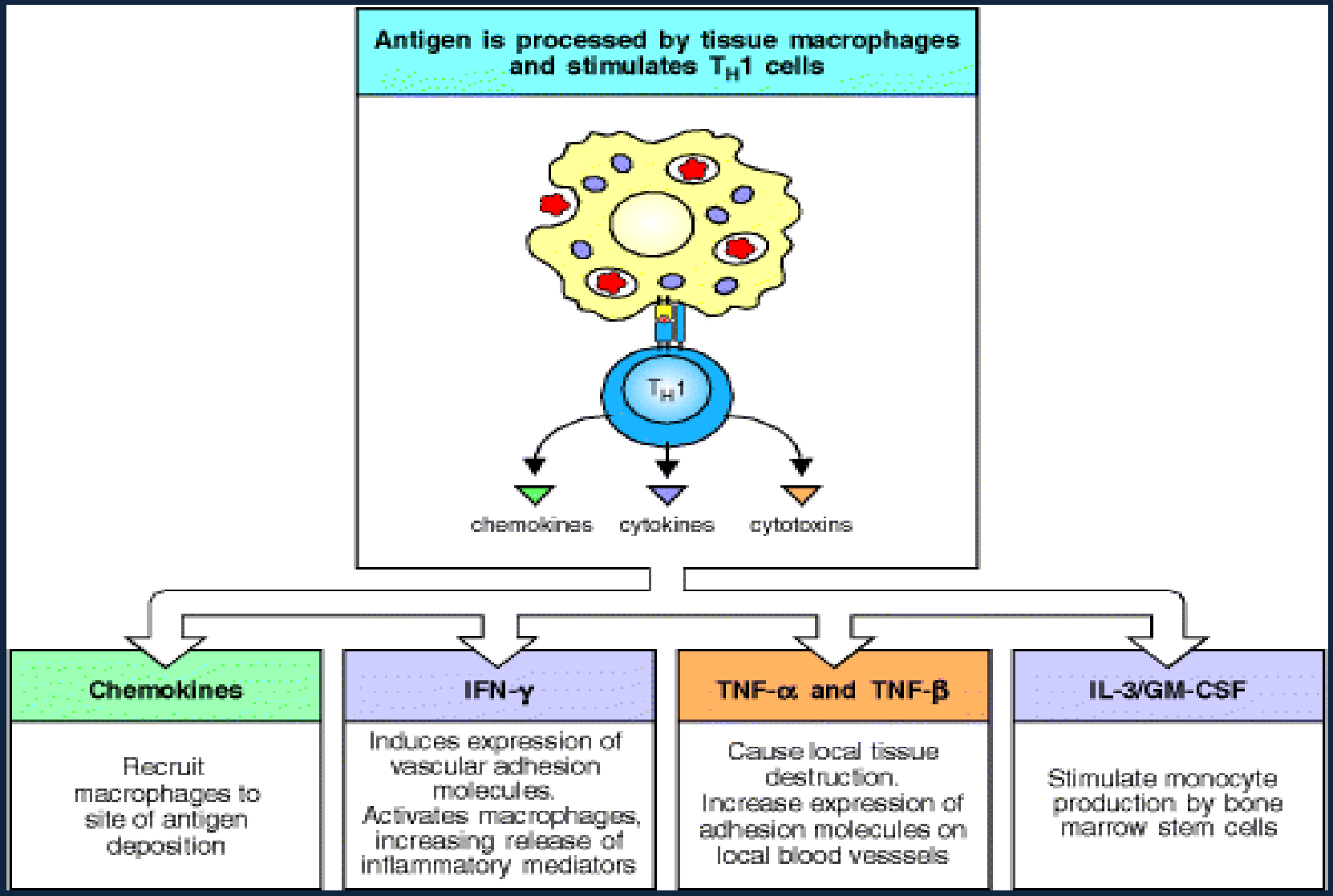
Demonstration of specific immune complexes in the blood or tissues by:

Immunofluoresence

# Type IV hypersensitivity reactions (Delayed Hypersensitivity)

- Features
- Cell mediated immune response
  - Antigen dependent T cell (CD4 generally and CD8 occasionally) activation via MHC Class I or II
- Activated macrophages
- Delayed onset (2-4 days)
- Abnormal cellular response
  - (Granuloma formation)

# Mediators released by $T_{DTH}$ cells

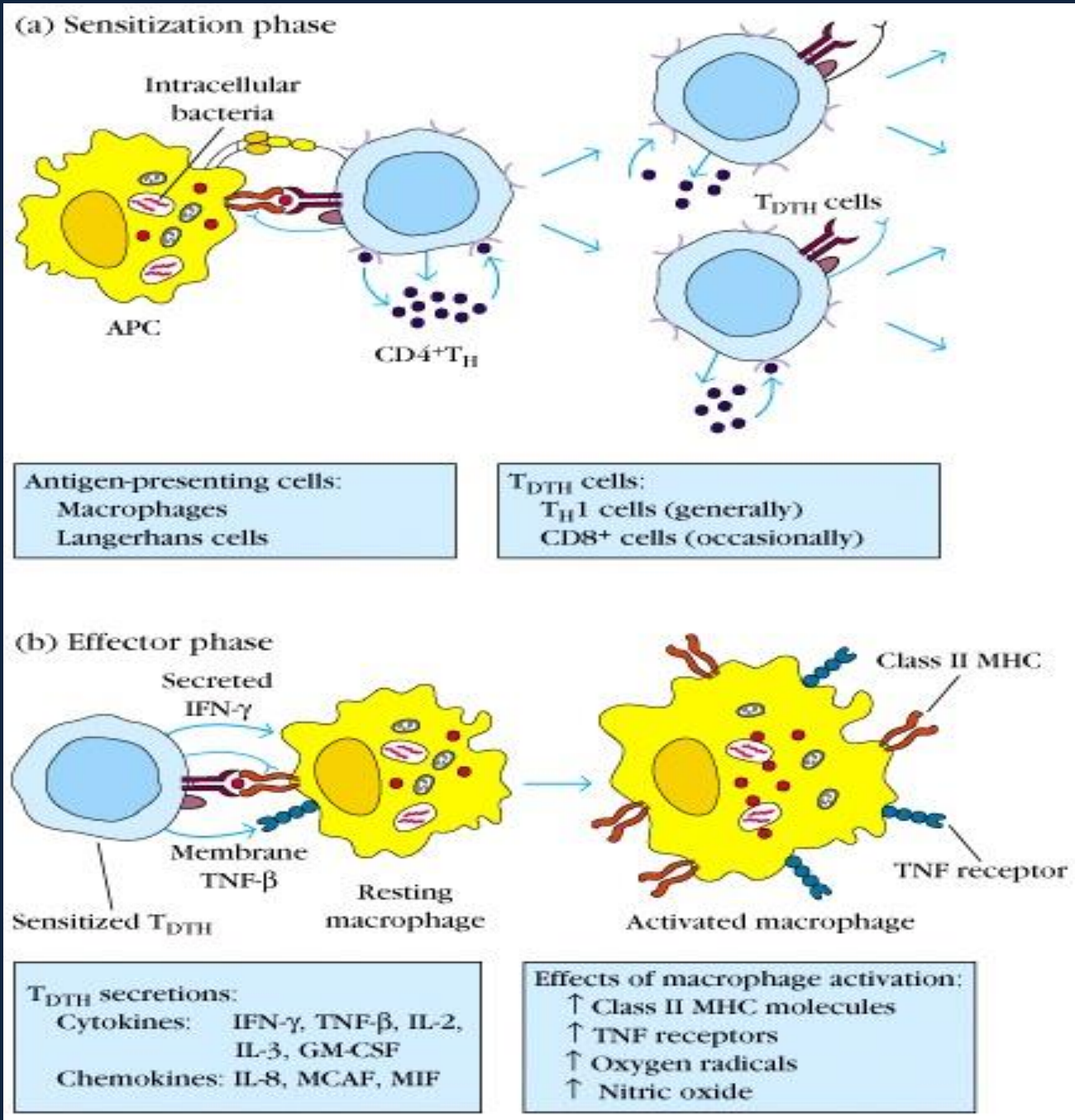


# Development of DTH Response

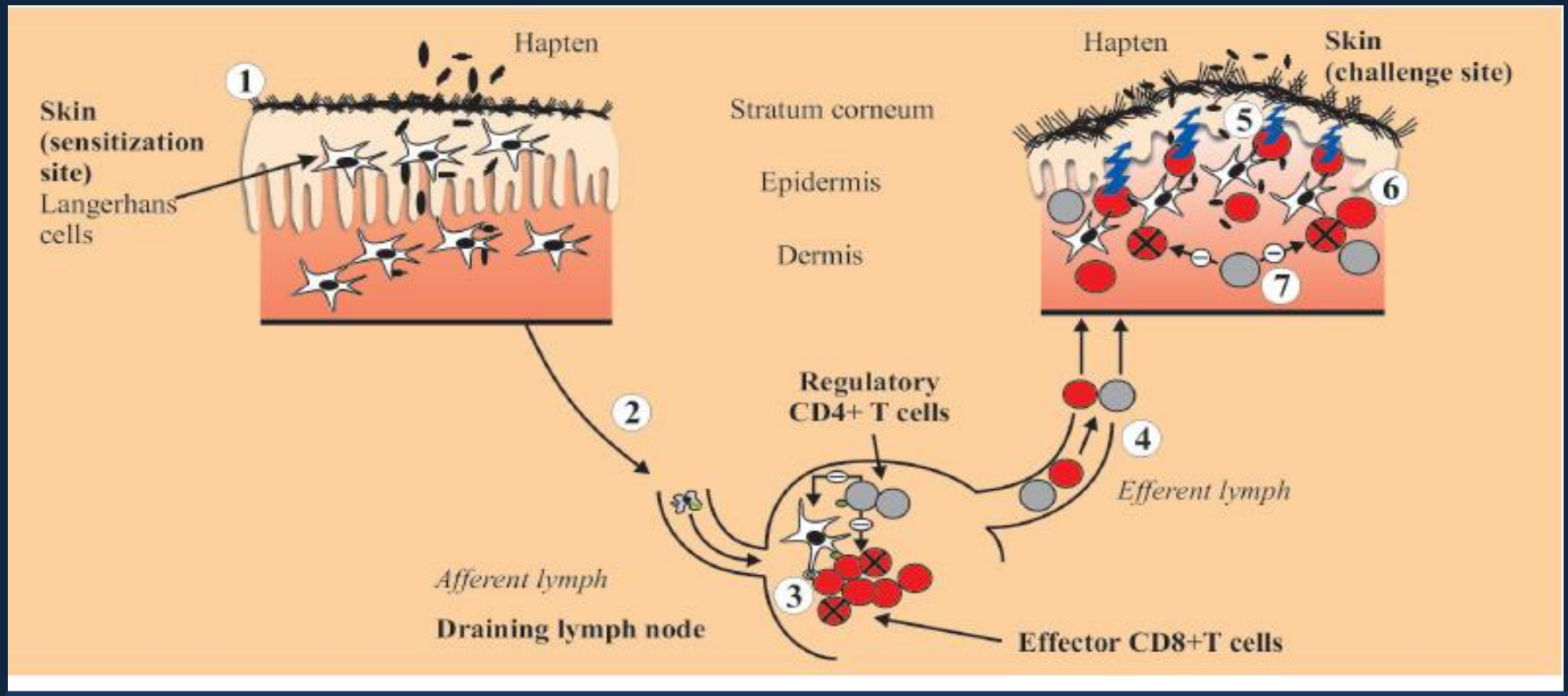
Sensitization phase:
1-2 week period

Effector phase:
24-72 hours

Effector cells (activated macs) act non-specifically

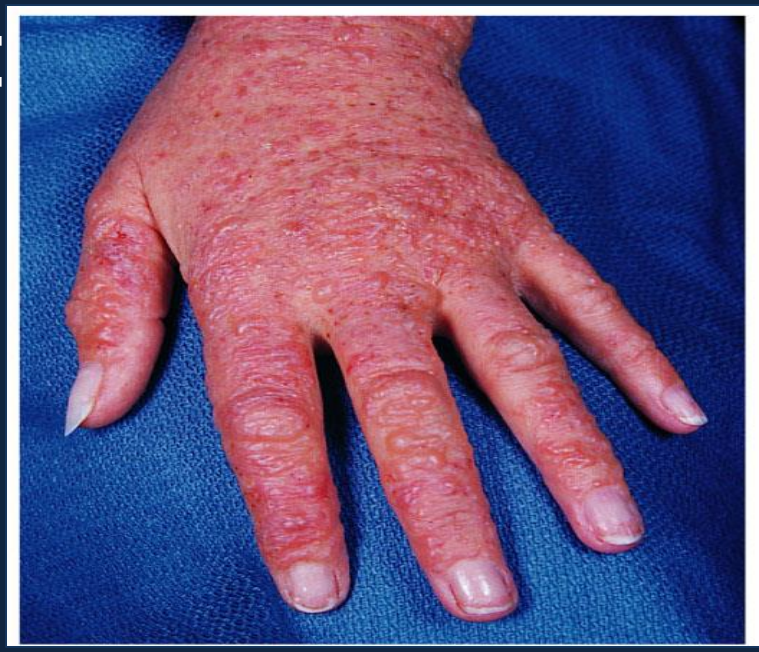


# Pathophysiology of Contact dermatitis.

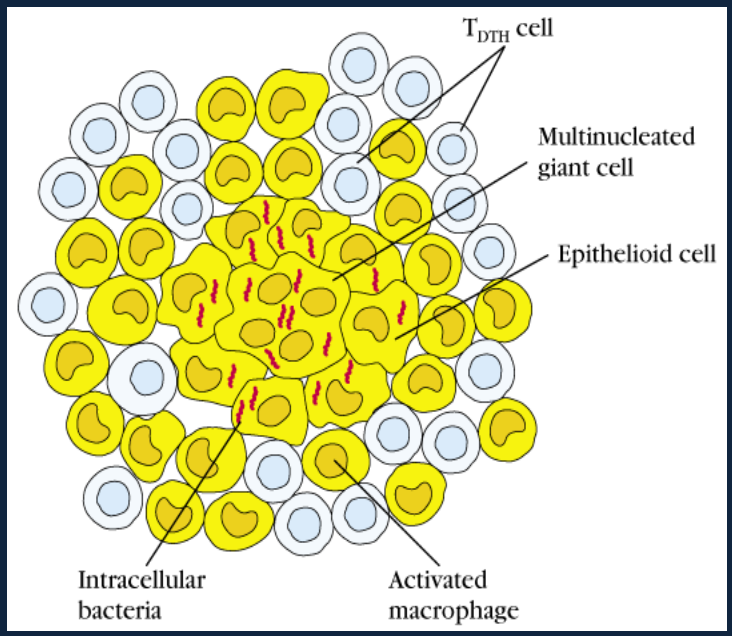


# Type IV clinical examples:

Contact dermatitis



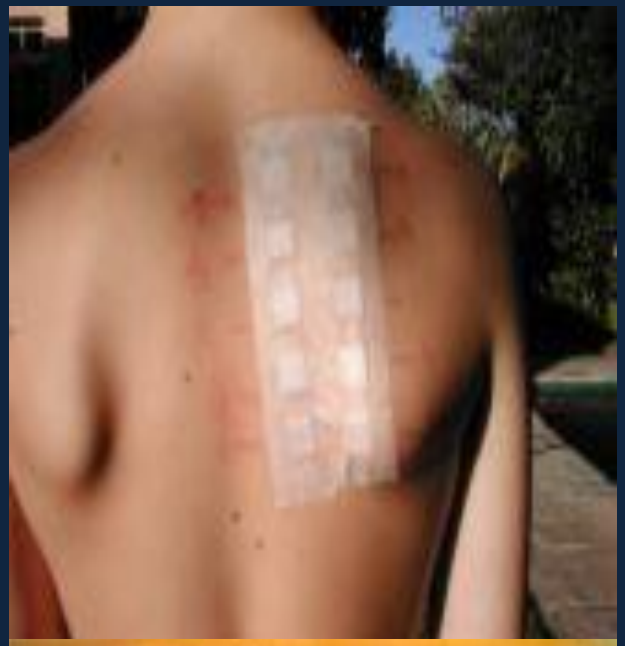
TB granuloma
(persistent antigen)

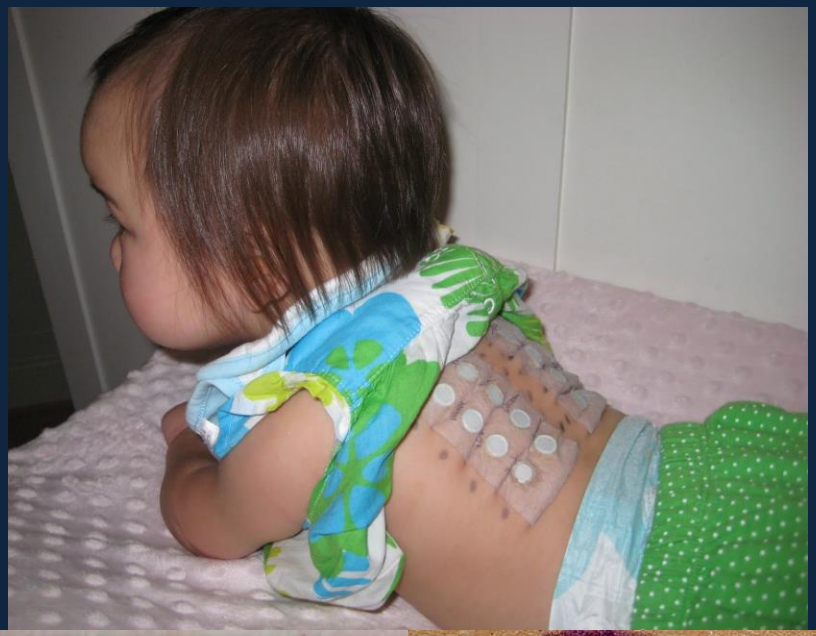


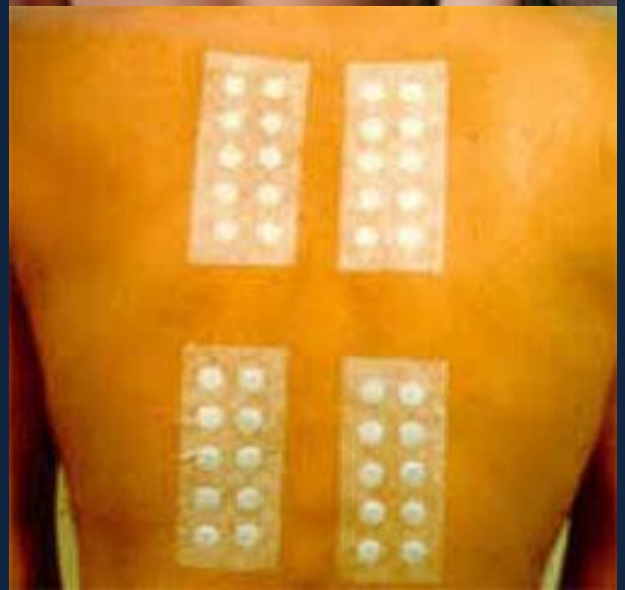
# Diagnosis (Type IV)

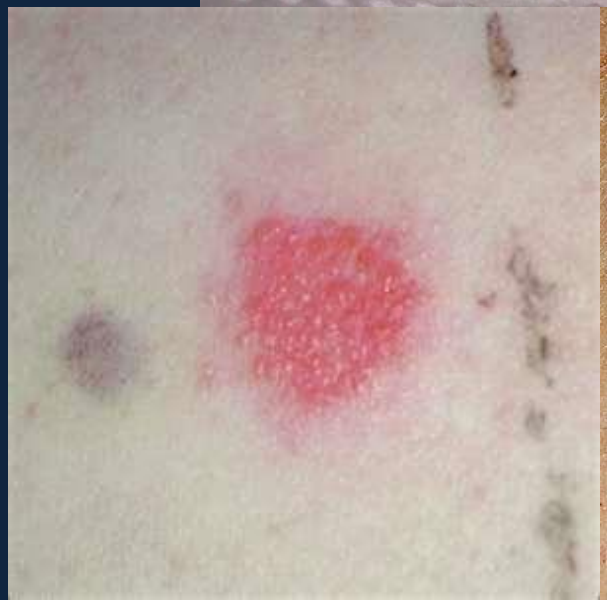
1. Delayed skin test (Mantoux test)
2. Patch test (Contact dermatitis)
3. Lymphocyte transformation test

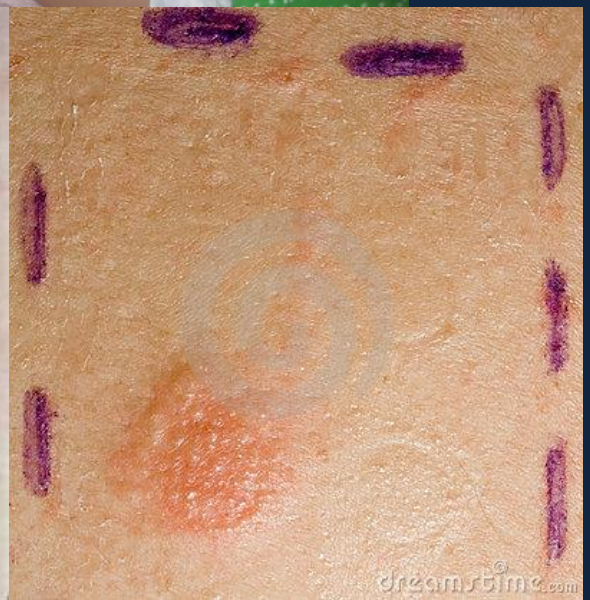
# Skin Patch Test











# Take Home Message

- 1. Type I (IgE), II (IgG) and III (IgG) hypersensitivity reactions are mediated by *antibodies* whereas Type IV hypersensitivity reaction is a *cell* mediated immune response.

- 2. Hypersensitivity reactions are *undesirable, excessive*, and *aberrant* immune responses associated with disorders such as allergy, autoimmunity and chronic inflammation.